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Polyurea microcapsules from isocyanatoethyl methacrylate copolymers

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((Additional Supporting Information may be found in the online version of this article.))

ABSTRACT

The synthesis of two types of isocyanate side chain containing copolymers, poly(methyl methacrylate-*co*-isocyanatoethyl methacrylate) (P(MMA-*co*-IEM)) and poly(benzyl methacrylate-*co*-isocyanatoethyl methacrylate) (P(BnMA-*co*-IEM)), which were synthesized by Cu(0)-mediated radical polymerization, is reported. Polymerization proceeded to high conversion giving polymers of relatively narrow molar mass distributions. The incorporation of the bulky aromatic groups in the latter copolymer rendered it sufficiently stable towards hydrolysis and enabled the isolation of the product and its characterization by ¹H and ¹³C NMR, and FTIR spectroscopy and SEC. Both P(MMA-*co*-IEM) and P(BnMA-*co*-IEM) were functionalized with dibutylamine, octylamine and (*R*)-(+)- α -methylbenzyl-amine, which further proved the successful incorporation of the isocyanate groups. Furthermore, P(BnMA-*co*-IEM) was used for the fabrication of liquid core microcapsules via oil-in-water interfacial polymerization with diethylenetriamine as crosslinker. The particles obtained were in the size range of 10 to 90 μ m in diameter independent of the composition of copolymer.

KEYWORDS: single electron transfer living radical polymerization (SET-LRP); oil-in-water interfacial polymerization; polyurea; isocyanate; microsphere

INTRODUCTION Liquid microcapsules have found use as carriers in personal care, agrochemical and drug delivery applications and as sensors and multi-compartment reactors.¹⁻³ They can be prepared through a range of techniques⁴, including self-assembly of functional polymers and templated approaches such as layer-by-layer assembly, which allow fine-tuning of the properties of the resulting capsules. Micro-capsules composed of polyurea have recently attracted significant interest, due to their ability to efficiently encapsulate numerous active ingredients.⁵⁻⁹ These microcapsules are usually prepared via an interfacial polymerisation in an emulsion.¹⁰⁻¹⁶ Recently, isocyanates have been employed to efficiently cross-link these microspheres as well as nanoparticles due to their high reactivity.^{10,17-20}

The extraordinary reactivity of isocyanates towards nucleophiles, which is attributed to the high electronegativity of oxygen and nitrogen generating a very electrophilic carbon centre, is of great interest as a synthetic tool. As a result, isocyanate functional groups are frequently employed as reactive intermediates.^{14,21,22} They are, however, highly sensitive to moisture. Dry reaction conditions, or the use of a glove box are frequently required to conduct successful reactions, or for storage. Isocyanate containing polymers are generally prepared through either modification of the initiator,^{23,24} incorporating an isocyanate containing monomer^{22,25} or post-polymerisation modification.²⁶ Chemical protection can be used to preserve isocyanate functionality during a reaction, followed by deprotection and subsequent modification.²⁷ Alternatively, Endo and coworkers incorporated

styrene monomers into polyisocyanates, which improved the stability of the isocyanate functional group.²⁸

Conventional free radical polymerization of isocyanatoethyl methacrylate (IEM) was introduced by Eick and coworkers with different monomers;²⁹ they suggested a successful synthesis was achieved as a $\nu_{\text{N}=\text{C}=\text{O}}$ absorbance was detected in FTIR. Reversible deactivation radical polymerizations (RDRP) provides several advantages over conventional free-radical polymerization, namely well-defined molecular mass and low molar mass dispersity³⁰ as well as high end group fidelity.³¹ Several different CRP techniques have been discovered in the last few decades, including reversible addition-fragmentation chain transfer polymerization (RAFT)³², atom transfer radical polymerization (ATRP)³³ and nitroxide-mediated polymerization (NMP)³⁴ and more recently Cu(0)-mediated radical polymerization (also known as single electron transfer living radical polymerization (SET-LRP)).^{30,35} The latter has been demonstrated to be a powerful technique for the polymerization of a wide range of vinyl monomers such as acrylamides,^{35,36} acrylates³⁷⁻³⁹ and methacrylates.⁴⁰⁻⁴²

With respect to isocyanate containing monomers, Hawker and coworkers, and Perrier and coworkers, reported the reversible deactivation radical polymerization of IEM *via* RAFT polymerization to prepare nanoparticles by intramolecular cross-linking and modification of isocyanate functional groups, respectively.^{18,25} To the best of our knowledge, Cu-mediated polymerization of this monomer has not yet been reported. However, with a lack of control over polymer composition, and high temperature requirements, there are still major barriers to the full exploitation of this monomer.

Herein, poly(methyl methacrylate-co-isocyanatoethyl methacrylate) (P(MMA-co-IEM)) and poly(benzyl methacrylate-co-isocyanatoethyl methacrylate) (P(BnMA-co-IEM)) are prepared using a copper(0) mediated

living polymerization system at ambient temperature. The copolymers are reacted with a diverse range of amines to confirm the presence of reactive isocyanates. The potential of stable P(BnMA-co-IEM) for the fabrication of microspheres via interfacial polymerization in emulsion is demonstrated. Characterization of the products has been carried out with ¹H, ¹³C NMR, Fourier transform infrared spectroscopy (FTIR) spectroscopy, size exclusion chromatography (SEC), and optical microscopy.

EXPERIMENTAL

Material

Acetone, ethyl α -bromoisobutyrate, dimethyl sulfoxide anhydrous, isocyanatoethyl methacrylate (IEM), methyl methacrylate (MMA), benzyl methacrylate (BnMA), deuterated chloroform (CDCl₃), deuterated chloroform anhydrous, 2-Isopropanol (anhydrous) (IPA), dimethyl sulfoxide anhydrous (DMSO), dichloromethane anhydrous (DCM), diethylenetriamine, poly(vinyl alcohol) (M_w 130,000 g mol⁻¹), copper(II) bromide, 35% aqueous hydrochloric acid, octylamine, dibutylamine and (*R*)-(+)- α -methylbenzylamine were purchased from Sigma-Aldrich UK. Carrier oil was purchased from Stephan Company. Me₆TREN was synthesized according to literature procedure.⁴³

Characterization

Size exclusion chromatography measurements were performed on an Agilent 390 MDS Multi-Detector GPC system (CHCl₃ + 2 % TEA Mixed C Column Set, 30°C flow rate 1 ml/min, narrow standard of PMMA was used calibration polymers between 955000 and 1010 g mol⁻¹ and fitted with a third order polynomial) by DRI detection. ¹H NMR (standard) and ¹³C NMR (long acquisition long delay) were recorded on a Bruker Avance III HD 400 MHz and Bruker Avance III HD 300 MHz with CDCl₃ and anhydrous CDCl₃ as the solvent. IR spectra were recorded on a Bruker Vector 22 FTIR spectrometer with OPUS software used to analyse absorbance data. Particle size in aqueous solution was obtained by Malvern

Instruments Mastersizer 2000 System and Olympus microscope (2x, 10x and 20x)

P(MMA_m-co-IEM_n) Polymerization

5 cm of copper wire was entwined with a magnetic stirrer bar, and placed into 3 mL of 35 % HCl solution for 5 minutes, washed with deionized water then acetone. Once dried, the cleaned wire was placed in a Schlenk tube containing CuBr₂ (5.70 mg, 2.55 x 10⁻⁵ mol (0.05 eq. relative to initiator) and sealed with a rubber septum. Ethyl α-bromoisobutyrate (75 μL, 5.11 x 10⁻⁴ mol, 1 eq.), 2-isocyanatoethyl methacrylate (0.36 mL, 2.55 x 10⁻³ mol, 5 eq.) and methyl methacrylate (2.45 mL, 2.29 x 10⁻² mol, 45 eq.) and anhydrous dimethyl sulfoxide (3 mL) were then added in to a Schlenk tube. The reaction mixture was degassed under a flow of N₂ for 15 minutes, then Me₆Tren (49.2 μL, 1.84 x 10⁻⁴ mol, 0.36 eq.) was added. The reaction was stirred for 5 hours, polymer solution was characterized by NMR, IR and SEC. ¹H NMR (300 MHz, CDCl₃, δ): 1.02 (m, CH₂), 1.82 (m, CH₃), 1.97 (m, CH₃ (monomer)), 2.63 (s, CH₃ (DMSO)), 3.48 (m, CH₂N) 3.59 (s, CH₃O), 3.75 (s, CH₃O (monomer)) 4.00 (s, CH₂OCO), 4.11 (m, CH₂OCO), 5.57 (s, CH, (monomer)), 5.65, (s, CH, (monomer)), 6.10 (s, CH, (monomer)), 6.18 (s, CH, (monomer)); IR (KBr): ν = 1750 (C=O), 2250 (NCO), 2950 (C-H); GPC_{THF}: M_n = 5900 g mol⁻¹, Đ = 1.58.

General modification of P(MMA-co-IEM) by amines

The polymerization mixture (1 mL) was transferred by cannula into 15 mL vial under positive N₂ pressure. Amine (0.5 mL, 3.86 x 10⁻³ mol) was directly injected into the reaction mixture. The reaction was left for 3 hours, and then THF (10 mL) was added. The solution was dialysed by MWCO 1k dialysis tubing against THF for 24 hours. The product was then precipitated in cold hexane and filtered by using Buchner filtration. Modified polymer was characterized by NMR, IR and SEC.

P(MMA_m-co-IEM_n) modification by dibutylamine

¹H NMR (400 MHz, CDCl₃, δ): 0.85 (m, 14H, CH₃),

0.94 (t, 6H, CH₃), 1.02 (m, 6H, CH₃), 1.34-1.53 (m, 8H, CH₂), 1.81 (m, 13H, CH₂), 3.21 (s, 4H, CH₂N) 3.50 (s, 2H, CH₂N), 3.60 (s, 17H, CH₃OCO), 4.08 (s, 2H, CH₂OCO); ¹³C NMR (400 MHz, CDCl₃, δ): 13.96 (s, CH₃), 16.49, 18.72 (s, C backbone), 20.21 (s, CH₂), 30.72 (s, CH₂), 39.85 (s, CH₂N), 44.55 (s, CH₂N), 51.83 (s, CH₃O), 54.39 (s, CH₃), 65.22 (s, CH₂OCO), 157.46 (s, NC=O), 177.81 (s, C=O); IR (KBr): ν = 2951 (C-H), 1725 (C=O), 1647 (C=O amide), 1239 (C-O); GPC_{THF}: M_n = 8300 g mol⁻¹, Đ = 1.37.

P(MMA_m-co-IEM_n) modification by octylamine

¹H NMR (400 MHz, CDCl₃, δ): 0.85-1.02 (m, 18H, CH₃), 1.27-1.48 (m, 9H, CH₂), 1.76-1.90 (m, 10H, CH₂), 3.18 (s, 2H, CH₂N) 3.53 (m, 2H, CH₂N), 3.60 (s, 14H, CH₃OCO), 4.03 (m, 2H CH₂OCO); ¹³C NMR (400 MHz, CDCl₃, δ): 14.13 (s, CH₃), 16.49, 18.72 (s, C backbone), 22.66, 26.95, 29.28, 31.84 (s, CH₂), 40.33 (s, CH₂N), 44.55 (s, CH₂N), 51.83 (s, CH₃O), 54.48 (s, CH₃), 65.40 (s, CH₂OCO), 158.18 (s, NC=O), 178.11 (s, C=O); IR (KBr): ν = 2951 (C-H), 1725 (C=O), 1647 (C=O amide), 1239 (C-O); GPC_{THF}: M_n = 8900 g mol⁻¹, Đ = 1.49.

P(MMA_m-co-IEM_n) modification by (R)-(+)-α-methylbenzylamine

¹H NMR (400 MHz, CDCl₃, δ): 0.84-1.02 (m, 21H, CH₃), 1.46 (m, 3H, CH₃), 1.81-1.94 (m, 16H, CH₂), 3.55 (m, 2H, CH₂N) 3.60 (s, 18H, CH₃OCO), 4.03 (s, 2H, CH₂OCO), 7.24-7.33 (m, CH aromatic); ¹³C NMR (400 MHz, CDCl₃, δ): 16.37, 18.71 (s, C backbone), 23.14 (s, CH₃), 38.70 (s, CH₂N), 44.54 (s, CH₃O), 51.83 (s, CH₃O), 54.20 (s, CH₃), 64.85 (s, CH₂OCO), 125.96 (s, CH aromatic), 128.52 (s, C aromatic) 157.78 (s, NC=O), 178.12 (s, C=O); IR (KBr): ν = 2950 (C-H), 1725 (C=O), 1645 (C=O amide), 1553 (C-C aromatic), 1365 (C-O); GPC_{THF}: M_n = 8800 g mol⁻¹, Đ = 1.54.

P(BnMA_m-co-IEM_n) Polymerization

5 cm of copper wire was entwined with a magnetic stirrer bar, and placed into 3 mL of 35 % HCl solution for 5 minutes, washed with deionized water then acetone. Once dried, the clean wire was placed in a Schlenk tube containing CuBr₂ (1.59 mg, 7.15 x 10⁻⁶ mol) (0.05 eq. relative to initiator) and sealed with a

rubber septum. Ethyl α -bromoisobutyrate (21 μ L, 1.43×10^{-4} mol, 1 eq.), 2-Isocyanatoethyl methacrylate (0.10 mL, 7.15×10^{-4} mol, 5 eq.), benzyl methacrylate (1.09 mL, 6.43×10^{-3} mol, 45 eq.) and anhydrous 2-Isopropanol (1.2 mL) were then added. The reaction mixture was degassed under a flow of N_2 for 15 minutes, then Me_6Tren (14 μ L, 5.15×10^{-5} mol, 0.36 eq.) was added. The reaction was stirred for 3 hours. Polymer was precipitated in cold hexane and isolated by filtering through a sintered glass funnel. The resultant off white powder was characterized by NMR, IR and SEC. 1H NMR (400 MHz, $CDCl_3$, δ): 0.73–0.92 (m, 15H, CH_3), 1.79–1.89 (m, 10H, CH_2), 3.40 (m, 2H, CH_2NCO), 4.00 (m, 2H, CH_2OCO), 4.95 (s, 10H, $PhCH_2OCO$), 7.40 (m, 25H, CH_2 aromatic); ^{13}C NMR (400 MHz, $CDCl_3$, δ): 16.71 (s, CH_2), 22.23 (s, CCH_3), 44.48 (s, CH_2N), 54.22 (s, CH_3), 66.82 (s, $PhCH_2O$), 68.29 (s, CH_2OCO), 128.26 (s, NCO), 128.57 (s, CH aromatic), 135.08 (s, C aromatic CH_2), 177.13 (s, $C=O$); IR (KBr): ν = 1500 (CH aromatic), 1750 ($C=O$), 2250 (NCO), 2950 ($C-H$); GPC_{CHCl_3} : M_n = 7700 $g\ mol^{-1}$, \bar{D} = 1.41.

General modification of $P(BnMA_m-co-IEM_n)$ by amines

$P(BnMA_{22}-co-IEM_2)$ (0.05 g, 1.14×10^{-5} mol) was added into a 15 mL vial which contained 1 mL anhydrous dichloromethane and magnetic follower. The desired amine (5.93×10^{-4} mol) was added and the reaction mixture stirred for 3 hours. Modified polymer was precipitated in cool hexane, and characterized by NMR, IR and SEC.

$P(BnMA_m-co-IEM_n)$ modification by dibutylamine

1H NMR (400 MHz, $CDCl_3$, δ): 0.73–0.95 (m, 27H, CH_3), 1.20–1.49 (m, 10H, CH_2), 1.70–1.89 (m, 16H, CH_2), 3.15 (s, 2H, NCH_2), 3.42 (s, 2H, CH_2NCO), 3.97 (s, 2H, CH_2OCO), 4.95 (m, 10H, $PhCH_2OCO$), 7.40 (CH_2 , 31H, aromatic); ^{13}C NMR (400 MHz, $CDCl_3$, δ): 13.56 (s, CH_3), 18.63, 16.18 (s, CH_2), 20.18 (s, CH_2), 27.81 (s, CH_2), 39.72 (s, CH_2N), 44.77 (s, CH_2N), 54.04 (s, CH_3), 66.78 (s, $PhCH_2O$), 67.80 (s, CH_2OCO), 128.55 (s, CH aromatic), 135.08 (s, C aromatic CH_2), 157.39 (s,

$NC=O$) 177.13 (s, $C=O$); IR (KBr): ν = 2958 ($C-H$), 1725 ($C=O$), 1650 ($C=O$ amide), 1454 ($C-C$ aromatic), 1368 ($C-O$); GPC_{CHCl_3} : M_n = 7900 $g\ mol^{-1}$, \bar{D} = 1.27.

$P(BnMA_m-co-IEM_n)$ modification by octylamine

1H NMR (400 MHz, $CDCl_3$, δ): 0.73–0.92 (m, 26H, CH_3), 1.26–1.45 (m, 14H, CH_2), 1.78–1.90 (m, 16H, CH_2), 3.14 (s, 2H, CH_2NCO), 3.44 (s, 2H, CH_2NCO), 3.97 (s, 2H, CH_2OCO), 4.88 (m, 15H, $PhCH_2OCO$), 7.40 (m, 37H, CH_2 aromatic); ^{13}C NMR (400 MHz, $CDCl_3$, δ): 14.14 (s, CH_3), 16.65, 18.72 (s, CH_2), 22.18, 22.66, 26.98, 26.98, 29.31, 30.45, 31.84 (s, CH_2), 40.39 (s, CH_2N), 44.78 (s, NCH_2), 54.46 (s, CH_3), 66.78 (s, $PhCH_2O$), 66.98 (s, CH_2OCO), 128.53 (s, CH aromatic), 135.09 (s, C aromatic), 158.07 (s, $NC=O$) 177.40 (s, $C=O$); IR (KBr): ν = 2930 ($C-H$), 1723 ($C=O$), 1652 ($C=O$ amide), 1454 ($C-C$ aromatic); GPC_{CHCl_3} : M_n = 7200 $g\ mol^{-1}$, \bar{D} = 1.31

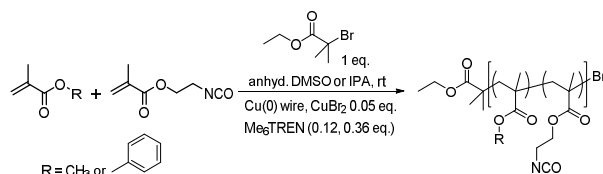
$P(BnMA_m-co-IEM_n)$ modification by (*R*)-(+)- α -methylbenzylamine

1H NMR (400 MHz, $CDCl_3$, δ): 0.72–0.92 (m, 24H, CH_3), 1.40 (d, 3H, CH_3), 1.78–1.88 (m, 16H, CH_3), 3.38 (m, 2H, CH_2N), 3.91 (m, 2H, CH_2OCO), 4.80 (m, 14H, $PhCH_2OCO$), 4.90 (m, 2H, $PhCHN$), 7.28 (m, 40H, CH_2 aromatic); ^{13}C NMR (400 MHz, $CDCl_3$, δ): 16.44, 18.58 (s, CH_2), 23.08 (s, CH_3), 39.59 (s, NCH_2), 44.77 (s, NCH_2), 54.53 (m, CH_2), 66.79 (s, $PhCH_2O$), 67.07 (s, CH_2OCO), 126.01, 128.55 (m, CH aromatic), 135.11 (s, C aromatic), 157.37 (s, $NC=O$), 177.27 (m, $C=O$); IR (KBr): ν = 2949 ($C-H$), 1724 ($C=O$), 1650 ($C=O$ amide), 1448 ($C-C$ aromatic), 1365 ($C-O$); GPC_{CHCl_3} : M_n = 6700 $g\ mol^{-1}$, \bar{D} = 1.36.

Microcapsule synthesis

$P(BnMA_m-co-IEM_n)$ copolymer (0.2 g) was added into 50 mL vial containing 2 mL anhydrous DCM. Neobee Carrier Oil (5 g) was added, followed by 18.4 mL of 1.3 % polyvinyl alcohol (Mowiol 18-88) aqueous solution. The mixture was homogenised at 2000 rpm for 3 minutes using an overhead dissolver disc. The mixture was transferred to 100 mL RBF and then stirred at 400 rpm using an overhead paddle mixer. To this, a 40% aqueous solution of diethylenetriamine (0.1 mL) was added drop-

wise into the reaction; the mixture was then left to stir at room temperature. After 1 hr the temperature was increased, 50 °C, after another hour the temperature was increased to 90 °C. Microcapsule size was determined by dynamic light scattering and optical microscopy.



Scheme 1 Schematic representation of SET-LRP of IEM.

RESULTS AND DISCUSSION

P(MMA-co-IEM) synthesis and modification

MMA and IEM (10 mol%) were copolymerized using a Cu(0)-mediated radical polymerization system with ethyl 2-bromoisobutyrate (EBiB) as initiator, anhydrous DMSO as solvent and a Cu(II)Br₂/Me₆Tren/EBiB ratio of 0.05:0.12:1 (Scheme 1)⁴⁴. Within three hours no further propagation occurred, at monomer conversions of 25 and 40 % (as determined by ¹H NMR) for MMA and IEM, respectively. This could be the result of a decrease in the reactivity of catalyst/ligand system over time. Subsequently, the concentration of Me₆Tren ligand was increased to 0.36 equivalents, resulting in a higher degree of polymerisation, with approximately 60% conversion for both monomers (Table S1). In addition, different feed ratios of IEM were also studied to determine the effect on the monomer conversion and dispersity (Figure S1). However, at high levels of isocyanate functionality in the copolymer, a lack of stability in the presence of moisture prevents this copolymer from being a suitable candidate to prepare microcapsules. higher degree of polymerisation, with approximately 60% conversion for both monomers (Table S1). In addition, different feed ratios of IEM were also studied to determine the effect on the monomer conversion and dispersity (Figure S1). However, at high levels of isocyanate

functionality in the copolymer, a lack of stability in the presence of moisture prevents this copolymer from being a suitable candidate to prepare microcapsules. The isocyanate reacts with water to generate carbamic acid which then decomposes to carbon dioxide⁴⁵ and a primary amine, which can form a urea bond with another isocyanate. Thus, a white precipitate of highly cross-linked polyurethane was observed within a few minutes of exposure polymer solution to moisture.

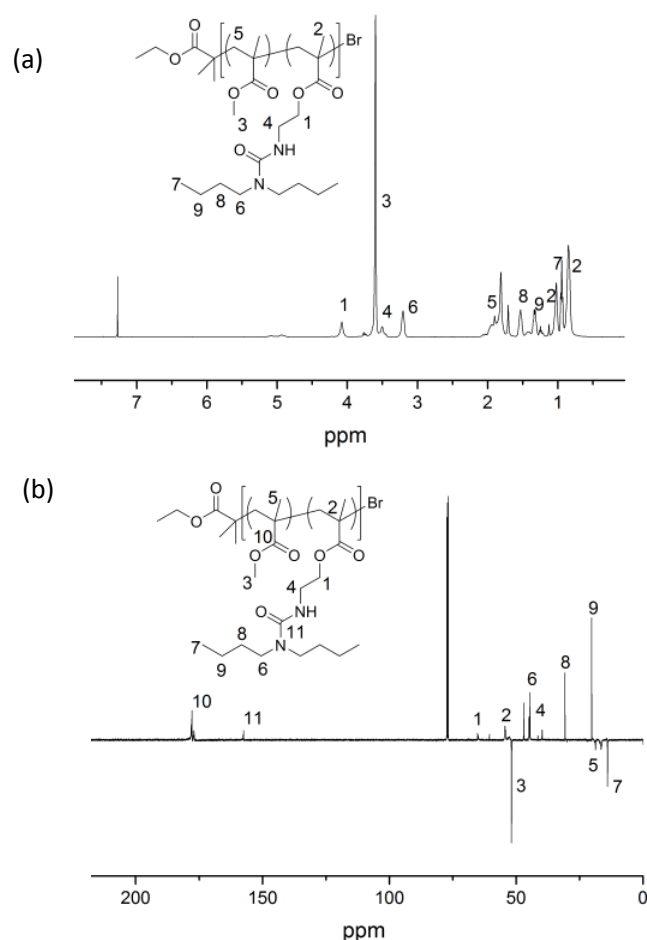


Figure 1 ¹H NMR (a) and ¹³C NMR (J-modulated) (b) of P(MMA₂₂-co-IEM₃) modified with dibutylamine (CDCl₃, 400 MHz).

Modification of the isocyanate group in the copolymer, in this case in-situ, is a simple method to confirm if isocyanates are still present and reactive following polymerization.

Table 1: Summary of SET-LRP result of BnMA/IEM copolymerization at room temperature after 3 hours.

Entry	Target DP		Conversion (%)		Polymer	$M_{n, \text{theo}}$ (g mol ⁻¹)	$M_{n, \text{GPC}}$ (g mol ⁻¹)	\bar{D}
	Overall	%IEM	BnMA	IEM				
1	50	0	45	-	PBnMA ₂₂	4071	3400	1.48
2	25	10	43	60	P(BnMA ₁₀ -co-IEM ₂)	2267	4100	1.61
3	50	10	49	40	P(BnMA ₂₂ -co-IEM ₂)	4381	7700	1.41
4	100	10	54	45	P(BnMA ₄₈ -co-IEM ₄)	9273	12700	1.51

Three different amines: dibutylamine, octylamine and (*R*)-(+)- α -methylbenzylamine were used to examine this. To this end, the P(MMA₂₂-co-IEM₃) copolymer (Entry 3 Table S1) solution was transferred directly after polymerization to the amine solution using a cannula under N₂ and left to stir for 3 hours. After purification, ¹H and ¹³C NMR spectroscopy were used to indicate successful modification by amines; Figure 1 (a) shows successful modification with dibutylamine and in the ¹³C NMR (Figure 1 (b)) spectra a new signal at 159 ppm can be attributed to the newly formed urea bond (Figure S2-S5 for octylamine and methylbenzylamine reactions). Furthermore, FTIR spectroscopy (Figure S6) confirmed the successful functionalisation, by disappearance of the characteristic $\nu_{\text{N}=\text{C}=\text{O}}$ vibration at 2250 cm⁻¹ in the product IR spectrum. Pleasingly, functionalisation had little effect on dispersity (Figure 2).

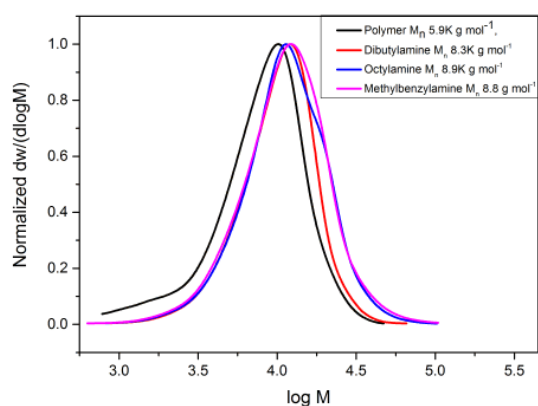


Figure 2 GPC traces of P(MMA₂₂-co-IEM₃) before and after modification by different amines, in THF eluent with DRI detection.

P(BnMA-co-IEM) synthesis and modification

In order to preserve the isocyanate functionality and allow isolation of the IEM copolymer, rapid monomer conversion and a straightforward purification protocol are required. DMSO is the most common solvent for Cu(0)-mediated radical polymerization, although a difficulty in removing this solvent is still a major drawback. Alternatively, isopropanol (IPA) is easier to remove while not affecting the dispersity of the resultant well-defined polymer, as has been shown with various acrylate, methacrylate and acrylamide monomers.⁴⁶⁻⁴⁸ In an attempt to prepare stable IEM copolymers, IEM was copolymerized with benzyl methacrylate (BnMA) in IPA using [CuBr₂]/[Me₆Tren]/[EBiB] = 0.05:0.12:1. The polymerization ceased within 5 hours, in line with the P(MMA-co-IEM) polymerization above, resulting in conversions of 10% and 70% of BnMA and IEM, respectively. No further increase in molecular weight, determined by SEC, was observed (Figure S7). However, monomer conversion was successfully increased in the presence of increased Me₆Tren concentration, thus a [CuBr₂]:[Me₆Tren] = 0.05:0.36 catalyst was employed.

Kinetic studies of P(BnMA-co-IEM) formation showed pseudo first-order kinetics and a linear increase in molar mass with monomer conversion, up to 90 minutes, as monitored by ¹H NMR spectroscopy (Figure 3, Figure S8 and Table S2). A perceptible drop in rate can be seen after 90 minutes, due to phase separation between polymer and monomer/solvent (Figure

S9). Polymerizations were left for up to 6 hours and interestingly, similar BnMA monomer conversion was detected for 2, 4 and 6 hours, while an increasing amount of IEM was consumed with time (90% at 6 hours) (Table S3). Unfortunately, as IEM monomer conversion significantly increased the dispersity of the copolymer also increased to $\bar{D} = 2.35$ (Figure S10). This could be due to termination reactions, of which disproportionation would dominate, resulting in a loss of control over the reaction. Likewise, considering the reactivity of the pendant isocyanate group, deviations in molecular weight and dispersity will occur due to enhancements in the occurrence of side reactions (i.e. crosslinking). Thus, it was decided that $[\text{CuBr}_2]:[\text{Me}_6\text{Tren}] = 0.05:0.36$ catalyst, and limiting the reaction time to 3 hours, were the optimal conditions to synthesize P(BnMA-co-IEM) with different monomer feed ratios (Table 1).

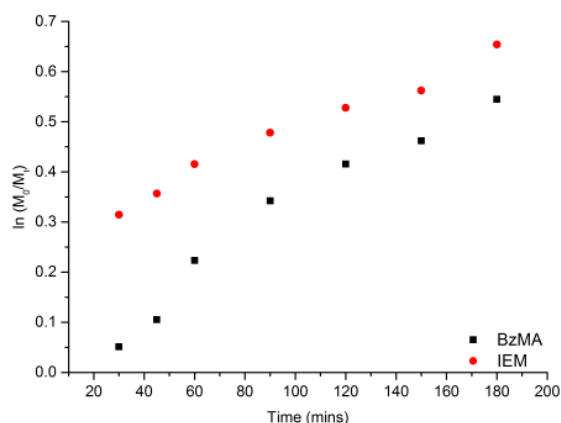


Figure 3 Kinetic plot for the synthesis of P(BnMA-co-IEM) with monomer conversion measured by ^1H NMR.

FTIR was used to determine the incorporation of the isocyanate functional group in to the copolymer. Strong transmittance of characteristic $\nu_{\text{N}=\text{C}=\text{O}}$ stretches at 2250 cm^{-1} demonstrates that the isocyanate group is still intact (Figure 4). We observe an acceptable control over molecular weight and dispersity (Figure 5). No significant differences in dispersity are observed for both the homopolymer and copolymer. The PBnMA

homopolymer has a uniform SEC trace, whereas the copolymer traces have a molecular weight shoulder and higher polydispersity, indicative of side reaction of isocyanate functional group (Figure S11). Although polymerizations were carried out under N_2 and using anhydrous solvents, reaction of the isocyanate group with water, with subsequent cross-linking could have occurred, despite every effort to exclude water and alcohols.

The use of BnMA as comonomer proved to have a beneficial effect on the stability of the copolymers, similar to the observation made by Endo.²⁸ Upon successful polymerization, the copolymer was isolated by precipitation into cold *n*-hexane (Figure S12 and S13). Further analysis of the isocyanate functionality was carried out post-purification, to ensure that the polymer would be suitable for preparing microcapsules. Purified P(BnMA₂₂-co-IEM₂) was functionalised with octylamine, dibutylamine and (*R*)-(+)- α -methylbenzylamine. The products were analysed by FTIR and NMR spectroscopy. An absence of a peak at 2250 cm^{-1} , indicative of isocyanate, and a detection of $\nu_{\text{C}=\text{O}}$ urea stretch at 1647 cm^{-1} shows that isocyanate functional groups in P(BnMA₂₂-co-IEM₂) were successfully modified by dibutylamine (Figure 4).

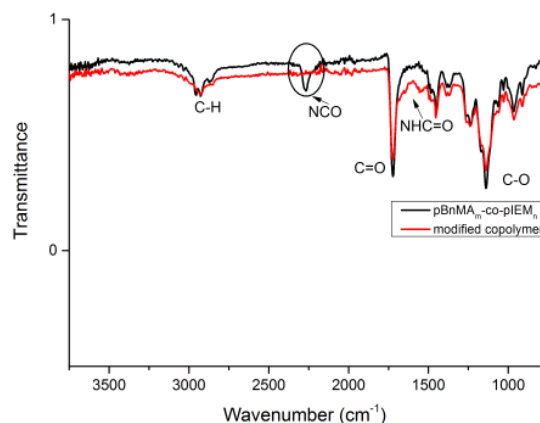


Figure 4 FTIR spectra of P(BnMA₂₂-co-IEM₂) and copolymer modified by dibutylamine.

^{13}C NMR shows the formation of a urea functional group (156.5 ppm) for all three modified samples, which was also confirmed by

^1H NMR (Figure S14–S18). The chemical shift of the methylene group in the copolymer modified by octylamine (Figure 6, position 11 and 12) indicates no variation of chemical shift when compared to non-functional $\text{P}(\text{BnMA}_{22}\text{-co-IEM}_2)$ (Figure S12). The molar mass of the amine-functionalised copolymer was slightly different from $\text{P}(\text{BnMA}_{22}\text{-co-IEM}_2)$, however, the observation that there is no change in the dispersity values indicates that no inter/intramolecular cross-linking occurred during modification and purification (Figure S19).

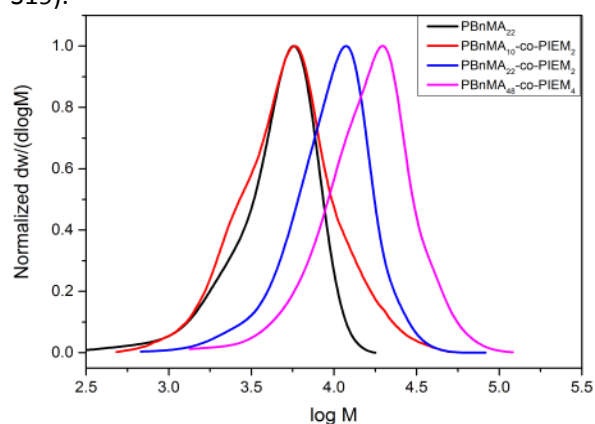


Figure 5 SEC trace of $\text{P}(\text{BnMA}_m\text{-co-IEM}_n)$ which is polymerized via SET-LRP in anhydrous IPA, in CHCl_3 eluent with DRI detection.

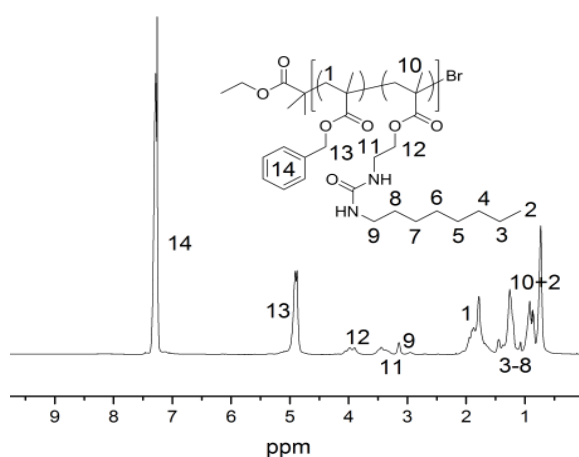
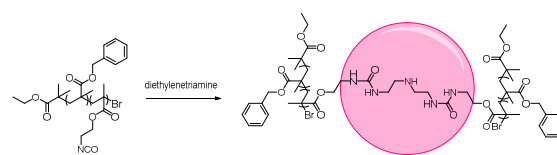


Figure 6 ^1H NMR (CDCl_3 , 400 MHz) of $\text{P}(\text{BnMA}_{22}\text{-co-IEM}_2)$ modified with octylamine.

Microcapsule synthesis



Scheme 2 Microcapsule fabrication via oil-in-water interfacial polymerization of $\text{P}(\text{BnMA}_m\text{-co-IEM}_n)$.

With this robust protocol for preparing isocyanate containing copolymers in hand, these polymers were taken on and used to prepare polyurea microcapsules *via* oil-in-water interfacial polymerization⁴⁹. To this end, $\text{P}(\text{BnMA}_m\text{-co-IEM}_n)$ was dissolved in anhydrous dichloromethane followed by the addition of carrier oil and stabiliser poly(vinyl alcohol) solution. Subsequently, the solution mixture was homogenised and cross-linked by addition of diethylenetriamine. The size of the resulting particles was determined by light optical microscope and dynamic light scattering. Variation of either the molecular weight of the copolymer, or percentage of isocyanate functionality, afforded no significant differences in particle size according to optical microscopy measurements. Exemplarily, Figure 7 shows that a range of differently sized particles from 10 to 90 μm in diameter, were prepared. This analysis was confirmed by Mastersizer laser diffraction measurements; a range of sizes of 20 to 100 μm microcapsules (Figure S20) were isolated from the slurry by spray drying (Figure S21a, S21b). FTIR spectroscopic analysis of these dried capsules showed a $\nu_{\text{N}=\text{C}=\text{O}}$ at 1650 cm^{-1} , and the absence of a characteristic isocyanate absorbance at 2250 cm^{-1} (Figure S22).

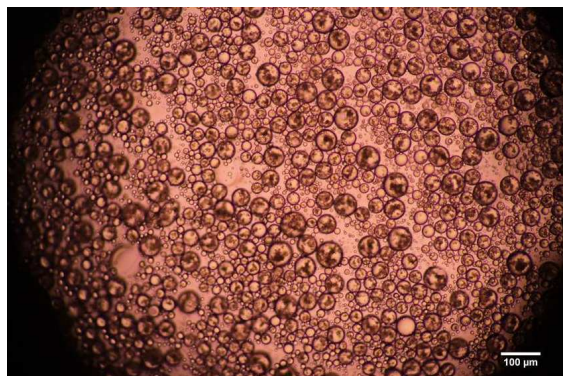


Figure 7 Optical microscope image of microcapsules obtained from p(BnMA₄₈-co-IEM₄).

CONCLUSIONS

Isocyanate functional copolymers were successfully synthesized *via* Cu(0)-mediated living radical polymerization (also known as SET-LRP) at ambient temperature. P(MMA-co-IEM) was prepared and modified with three different amines. In order to improve the stability of the isocyanate functional group, benzyl methacrylate was incorporated into the polymerization protocol. This allowed to prepare stable copolymers which can be isolated through a simple polymer purification strategy. The isocyanate-containing copolymer was taken on and used for the fabrication of polyurea microcapsules *via* oil in water interfacial polymerization. Interestingly, particle sizes showed no significant differences when copolymers of different molecular weights and isocyanate compositions were used. In conclusion, we introduce a facile synthetic method to prepare moisture stable isocyanate containing copolymers and demonstrate their use to fabricate functional polyurea microcapsules.

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GRAPHICAL ABSTRACT

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Polyurea microcapsules from isocyanatoethyl methacrylate copolymers

Poly(benzyl methacrylate-*co*-isocyanatoethyl methacrylate) (p(BnMA-*co*-IEM)) copolymers which are sufficiently stable towards hydrolysis were synthesized by Cu(0)-mediated radical polymerization. The isocyanate side groups were exploited for post-polymerization modifications with different model amine compounds and for the fabrication of liquid core microcapsules via oil-in-water interfacial polymerization.

